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Obsessive-compulsivity and working memory are associated with differential prefrontal cortex and insula activation in adolescents with a recent diagnosis of an eating disorder

Samantha J. Brooks [a,b,*], Linda Solstrand Dahlberg [a], Ingemar Swenne [c], Marianne Aronsson [c], Sanaz Zarei [a], Lina Lundberg [a], Josefin A. Jacobsson [a], Mathias Rask-Andersen [a], Helena Salonen-Ros [d], Agneta Rosling [d], Elna-Marie Larsson [e], Helgi B Schiöth [a]

[a] Department of Neuroscience, Functional Pharmacology, Uppsala University, Uppsala, Sweden
[b] Deptartment of Psychiatry and Mental Health, University of Cape Town, Cape Town, Western Cape, South Africa
[c] Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden
[d] Department of Neuroscience, Child and Adolescent Psychiatry, Uppsala University, Sweden
[e] Department of Radiology, Uppsala University, Uppsala, Sweden

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ABSTRACT

The role of rumination at the beginning of eating disorder (ED) is not well understood. We hypothesised that impulsivity, rumination and restriction could be associated with neural activity in response to food stimuli in young individuals with eating disorders (ED). We measured neural responses with functional magnetic resonance imaging (fMRI), tested working memory (WM) and administered the eating disorders examination questionnaire (EDE-Q), Barratt impulsivity scale (BIS-11) and obsessive-compulsive inventory (OCI-R) in 15 adolescent females with eating disorder not otherwise specified (EDNOS) (mean age 15 years) and 20 age-matched healthy control females. We found that EDNOS subjects had significantly higher scores on the BIS 11, EDE-Q and OCI-R scales. Significantly increased neural responses to food images in the EDNOS group were observed in the prefrontal circuitry. OCI-R scores in the EDNOS group also significantly correlated with activity in the prefrontal circuitry and the cerebellum. Significantly slower WM responses negatively correlated with bilateral superior frontal gyrus activity in the EDNOS group. We conclude that ruminations, linked to WM, are present in adolescent females newly diagnosed with EDNOS. These may be risk factors for the development of an eating disorder and may be detectable before disease onset.

1. Introduction

Current clinical interventions and treatment for eating disorders (ED) are primarily focused on diagnostic criteria as defined by DSM-IV (American Psychiatric Association, 2013). This is problematic, since up to 60% of the patients admitted to ED clinics are diagnosed with an eating disorder not otherwise specified (EDNOS) (Turner and Bryant-Waugh, 2004; Fairburn et al., 2007). EDNOS patients are individuals who display disordered eating behaviours and symptoms with clinical severity, but who fail to fulfil the criteria of anorexia nervosa (AN) and bulimia nervosa (BN) as defined in DSM-IV. The symptoms displayed in EDNOS patients vary, and there may include a mixture of features of both AN and BN. In a recent study, Keel et al. compared ED criteria set by the DSM-IV and the criteria, which at the time of publication, were proposed revisions for DSM-5. The authors found that by using the less strict criteria for AN and BN set by the DSM-5, there was a significant reduction in EDNOS cases (Keel et al., 2011). This makes interpretation and application of the evidence base for treatment difficult, and emphasises the importance of identifying early risk factors independent of diagnostic categorisation which would help to improve treatment before the development of a chronic ED, which may be harmful to brain function if left untreated.

Core traits witnessed in people diagnosed with ED include unhealthy attempts at restriction of food, as well as cognitive disturbances such as perfectionism, obsessional thinking, lack of central coherence and anxiety (Nilsson et al., 2008; Raney et al., 2008). Childhood anxiety is closely linked to the severity of symptoms

* Corresponding author at: Deptartment of Psychiatry and Mental Health, University of Cape Town, Cape Town, Western Cape, South Africa. Tel.: +27 021 4045427.
E-mail address: drsamanthabrooks@gmail.com (S.J. Brooks).

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displayed in patients with fully developed eating disorders, and the lifetime prevalence of obsessive-compulsive disorder (OCD) (OCD is considered an anxiety disorder according to the DSM-IV) or social phobia in people with a main diagnosis of AN has been reported to be between 23% and 75% (Halmi et al., 1991; Deep et al., 1995; Godart et al., 2002; Godart et al., 2003; Swinbourne and Touyz, 2007; Raney et al., 2008). AN patients frequently display obsessive and compulsive behaviour concerning weight, shape and eating (Fairburn and Harrison, 2003), such as excessively exercising and compulsively striving for thinness. Conversely, BN patients are impulsive, with a cognitive inability to restrict their eating behaviour in the longer term. Impulsivity can be described as individuals' predisposition to perform actions based on instinct, or with little or no foresight. Compulsivity is a related construct, and can be defined as carrying out an action as a response to the impulse, without considering subsequent consequences. Obsessive worry and rumination are impulsive/compulsive cognitive traits that coincide with the behaviours observed in those with eating disorders (Startup et al., 2013), particularly in an adolescent group where the disorder is just manifesting.

Little is known about the neurobiological underpinnings of EDNOS in adolescents, and the only functional magnetic resonance imaging (fMRI) study to date that has examined this population is in a group of adults (but not adolescents) who met subthreshold criteria for BN (Celone et al., 2011). Results showed reduced processing efficiency in fronto-striatal learning systems, which may be linked to cognitive rumination, in EDNOS compared with controls. However, it is still not known whether fronto-striatal circuitry is aberrant in adolescents with a diagnosis of EDNOS. Furthermore, given that OCD symptoms, cognitive rumination and worrying thoughts about shape, weight and eating are core cognitive traits that often predate the onset of an underweight status, it is relevant to examine the neural correlates of these traits in an EDNOS population.

One neuropsychological process that likely is linked to cognitive rumination and obsessional thinking is working memory (WM), particularly if excessively activated. WM is the ability to hold in mind a cognitive strategy while attending to immediate stimuli, and is associated with dopaminergic activity and genetic susceptibility in fronto-striatal brain circuitry (Bäckman and Nyberg, 2013; Logue and Gould, 2014). Only 10 studies to date have examined WM performance in those with eating disorders, and none in EDNOS, with mixed findings (Seed et al., 2002; Fowler et al., 2006; Dickson et al., 2008; Castro-Fornieles et al., 2010; Hatch et al., 2010; Nikendei et al., 2011; Brooks et al., 2012a; Pruis et al., 2012; Kothari et al., 2013; Lao-Kaim et al., 2014). Six of these studies reported better WM abilities in those with eating disorders (Dickson et al., 2008; Hatch et al., 2010; Brooks et al., 2012a; Pruis et al., 2012; Kothari et al., 2013). Three studies reported no difference (Fowler et al., 2006; Nikendei et al., 2011;Lao-Kaim et al., 2014), and one reported worse performance (Seed et al., 2002). Additionally, two studies were able to demonstrate that eating disorder stimuli (images of food and negatively rated bodies) disrupt WM performance (Brooks et al., 2012a; Pruis et al., 2012), and one study showed a general interference with WM when any stimuli were presented (Dickson et al., 2008). Of these 10 studies, only three examined brain activation in adults with eating disorders, and those studies found differences in parietal, temporal and fronto-striatal circuitry (Castro-Fornieles et al., 2010; Pruis et al., 2012; Lao-Kaim et al., 2014). WM is therefore a pertinent cognitive function to measure in adolescents with EDNOS, as it likely supports obsessive ruminations about shape, weight and eating that are prevalent in individuals with eating disorders.

Thus, the aim of this study was to uncover aspects of neuropathology that occur in the early phase of an ED, associated with the core traits of cognitive rumination, particularly during the neural processing of food stimuli. We measured brain activity during the presentation of food images, impulsivity, restraint, obsessive-compulsive symptoms and WM in both EDNOS and healthy adolescents. We hypothesised that measures of impulsivity would correlate with activity in reward system structures such as the dorsal striatum. We also predicted that restraint, obsessive-compulsive symptoms and WM scores in the EDNOS group would correlate with frontal activation, more specifically with activity in fronto-striatal circuitry.

2. Methods

2.1. Subjects

The subjects included in the analyses were 15 adolescent females with newly diagnosed eating disorders (ages 13–17, mean age: 15). The patients had features of anorexia nervosa but were categorised as EDNOS because newly diagnosed patients with eating disorders are known to veer between diagnostic subtypes during the first 6 months, and disorder-related behaviours frequently change (Fairburn et al., 2007; Brooks et al., 2012b). The 15 EDNOS subjects were recruited by the Eating Disorder Unit of the Department of Child and Adolescent Psychiatry at Uppsala Hospital, Sweden. Twenty healthy age-matched controls (HC) (ages 13–17, mean age: 14.2) were recruited from local schools in Uppsala, Sweden. The participants gave written consent to participate, and the study was approved by the local ethics committee. The HC group was screened for any diagnoses that were not detected by school personnel before study recruitment. This screening was carried out by a trained researcher administering a short version of a structured clinical interview for DSM disorders (SCID). For all subjects the exclusion criteria were as follows: comorbidity (for EDNOS patients), psychiatric or neurological disorders (for the control group), left-handedness, metallic implants, claustrophobia and use of psychotropic medication. Three additional EDNOS patients were recruited but were not able to take part because of left-handedness or metallic implants, and one refrained to take part as her clinician deemed her too ill to participate. Thirteen additional controls were also recruited but excluded due to previous mental illnesses, claustrophobia, medication and metallic implants. All subjects answered a selection of questionnaires and underwent a scanning procedure where they were presented with both high- and low-calorie food images, explicitly and subliminally. The subjects were instructed to imagine eating the food displayed on the images. The neural activation in response to these images was recorded in the scanner.

2.2. Measurements

The traits were measured by self-report questionnaires administered to the subjects before the scanning. Restraint was measured by the eating disorders examination questionnaire (EDE-Q) (Fairburn and Beglin, 1994) consisting of 36 questions. This questionnaire is divided into the following four subscales: restraint, concerns over eating, shape and weight. The questionnaire assesses how much time is spent worrying about these attributes. Answers are based on a seven-point scale ranging from 0 ('not at all') to 6 ('a lot').

The severity of obsessive/compulsive symptoms was measured with the obsessive-compulsive inventory-revised (OCI-R) (Foa et al., 2002). The OCI-R measures a construct that bridges impulsivity and restraint. The questionnaire consists of 18 questions assessing each of the subscales, i.e., checking, hoarding, neutralising, obsessing, ordering and washing. Answers are based on a six-point scale ranging from 0 ('not at all') to 5 ('extremely much').

The Barratt impulsiveness scale 11 (BIS-11) (Patton et al., 1995) was used to measure the subjects' personality construct of impulsivity. This questionnaire is one of the most commonly used questionnaires to measure impulsivity and its relationship to clinical conditions. The BIS consists of six subscales and 30 questions. Each answer is based on a four-point scale ranging from 'almost never' to 'almost always'. The subscales include self-control, perseverance, cognitive instability, cognitive complexity, motor and attention.

In this study the subjects underwent a working-memory task on-line in the scanner. This was the 1-back task (n-back task; Kirchner, 1958) in which the participants were shown different letters on the screen while being scanned. When one letter appeared two times in a row, they had to press a button. Reaction time (RT) and accuracy were recorded.

2.3. Image acquisition

Structural and functional brain images were acquired with a Philips 3-Tesla instrument (Achieva, Philips Healthcare, Best, Netherlands) using a standard head coil. During the T2-weighted echo-planar imaging (EPI) sequence, 125 volumes were registered with whole brain coverage of 30 slices (slice thickness = 3 mm; 1 mm gap, interleaved scan order, in-plane resolution: (3 mm × 3 mm), repetition time (TR) = 3000 ms; echo time (TE) = 35 ms, flip angle = 90°). The food images were presented